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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/724,397	12/01/2003	David M. Goldenberg	330687	8892

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PATENT DOCKETING
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EXAMINER	
SAMALA, JAGADISHWAR RAO	
ART UNIT	**PAPER NUMBER**
1618	

DATE MAILED: 10/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/724,397	GOLDENBERG ET AL.	
	Examiner	Art Unit	
	Jagadishwar R. Samala	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Application Status

1. Applicant's response to the Office Action was acknowledged on December 1, 2003.

Claim Disposition

2. Claim(s) 1-14 is/are pending and are under examination.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1-6, 8-10 and 12-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Behr (WO 96/29087) in view of Jones (Nucl. Med. & Biol., 1996; Vol. 23,105-113) and Geerlings (US 5,641,471).

Behr discloses a radioimmunoconjugate comprising a cytotoxic reagent for radioimmunotherapy or radioimmunodiaganostic, such as, which includes a molecule with a radioisotope binding site linked to an antigen binding fragment of an antibody which binds a tumor associated antigen and at least one clearing agent which is an amino acid or peptide bearing an amino basic group (i.e., D-Lysine or D,L-Polylysine), see abstract, page 3, lines 1+, pages 7-8 and examples.

Behr fails to disclose cytotoxic reagent wherein additional metal-chelating clearing agent is included therein. However, the use of metal-chelating clearing agents for methods of radioimmunotherapy or radioimmunodiagnostic is well known in the art as shown by Jones.

Jones discloses that chelating agents (i.e., dithiol chelating agents; DMPS and DMSA) as potential adjuvants to radioimmunotherapy agents (e.g. radiolabeled antibodies) because the addition of a chelating agent as a clearing agent provides the advantage of reducing or preventing radiotoxicity, which is a side effect of radioimmunotherapy, see abstract and Introduction, page 105.

It would have been obvious to one of ordinary skill in the art to modify the cytotoxic reagent disclosed by Behr to include a chelating agent as an additional clearing agent because Jones teaches that chelating agents are useful as potential adjuvants in radiolabeled antibody compositions because they provide the advantage of reducing or preventing radiotoxicity (e.g., a side effect of radioimmunotherapy). One of ordinary skill in the art would have been motivated to include the chelating agent as an additional clearing agent in the cytotoxic reagent disclosed by Behr because the chelating agent taught by Jones, while having a similar effect as a clearing agent , provide an additional and separate advantage as compared to the clearing agent disclosed by Behr. For example, Behr teaches that the clearing agent reduces renal uptake of the radiolabled monoclonal antibody fragments (i.e., to both reduce toxicity and increase specificity), while the clearing agent taught by Jones provides the additional advantage of removing free radiometal, thereby reducing or preventing

toxicity. It is well documented in the prior art about the use of radioimmunoconjugates for radioimmuno therapy and most suited for their potential therapeutic uses like micrometastases of various cancers, cellular cancers like leukemia and thereof (see, Geerlings, abstract and column 7, lines 15+).

5. Claims 7 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Behr (WO 96/29087) in view of Jones (Nulc. Med. & Biol., 1966 Vol.23, 105-113), as applied to claims 1-6, 8-10 and 12-14 above, and further in view of Griffiths (WO 96/40245).

Behr, as modified by Jones, teaches a cytotoxic agent comprising both an amino acid and metal-chelating agent, but fails to teach that an anti-idiotypic antibody clearing agent (i.e., directed to the radioactive binding molecule) is included therein.

Griffiths discloses a radioimmunoconjugate comprising a cytotoxic beta emitting radionuclide bound to an tumor antigen-binding fragment of an antibody, see abstract and page 7, line 23+ and page 11, lines 38+ and example 15 (e.g., Y-90). Various chelates (e.g., DOTA) are used to bind the radionuclide, see example 11. The compositions further includes one or more clearing agents including an antiidotypic antibody, non-antibody species (e.g.,peptides,etc.), galactosylated clearing agents, etc., see pages 9-10. Griffiths teaches that the addition of a clearing agent improves the target specificity of the radioimmunoconjugate in vivo, see abstract and pages 9-11. Griffiths specifically teaches the use of more than one clearing agent in multiple step methods, see page 10.

It would have been obvious to one of ordinary skill in the art to further modify the kits disclosed by Behr, as modified by Jones, to further include to include an antibody clearing agent (as claimed) because such clearing agents are well known in the art for improving the target specificity of a radioimmunoconjugate, as shown by Griffiths. One of ordinary skill in the art would have been motivated to include this additional clearing agent in the cytotoxic reagent disclosed by Behr because an antibody clearing agent, as taught by Griffiths, provides an additional and separate advantage as compared to the clearing agents disclosed by Behr (as modified by Jones), and Griffiths teaches advantages of using multiple clearing agents.

6. Claims 1-6, 8-10 and 12-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over any one Buchsbaum (US 4,831,122) or Behr (WO 96/29087) in view of Jones (Nucl. Med. & Biol., 1996; Vol. 23,105-113) and further in view of Griffiths (WO 96/40425).

Buchsbaum or Behr discloses a radioimmunocounjugate comprising a cytotoxic beta emitting radionuclide bound to an tumor antigen-binding fragment of an antibody (e.g., a Feb' fragment of IgG), see abstract and column 3, lines 42+ and claim 6. The radionuclide includes Y-90, etc., see column 4, lines 44+. The radionuclide may be bound using DTPA, see column 3, line 27.

Bachsbaum or Behr fails to disclose cytotoxic reagent wherein additional metal-chelating clearing agent is included therein. However, the use of metal-chelating

clearing agents for methods of radioimmunotherapy or radioimmunodiagnostic is well known in the art as shown by Jones.

Jones discloses that chelating agents (i.e., dithiol chelating agents;DMPS and DMSA) as potential adjuvants to radioimmunotherapy agents (e.g. radiolabeled antibodies) because the addition of a chelating agent as a clearing agent provides the advantage of reducing or preventing radiotoxicity, which is a side effect of radioimmunotherapy, see abstract and Introduction, page 105.

Although Buchsbaum or Behr in view of Jones teaches most elements required by the claims, they fail to teach about clearing agent.

Griffiths discloses radioimmunoconjugates and teaches that the addition of a clearing agent thereto improves the target specificity of the radioimmunoconjugate in vivo, see abstract and pages 9-11. Griffiths specifically teaches the use of more than one clearing agent in multiple step methods, see page 10.

It would have been obvious to one of ordinary skill in the art to modify the compositions disclosed by Bachsbaum, Behr or Jones to include clearing agents in cytotoxic beta emitting reagent of radioimmunoconjugate because Griffiths teaches that the inclusion of a clearing agent improves the in vivo targeting of the radioimmunoconjugate. Also, it would have been obvious to one of ordinary skill in the art to include the radioimmunoconjugates for radioimmuno therapy because it is well known in the art that such radioimmunoconjugates can be practicalized to improve the methods for diagnosing or treating patients using improved clearing agents as shown by Griffiths.

Conclusion

1. No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jagadishwar R. Samala whose telephone number is (571)272-9927. The examiner can normally be reached on 8.30 A.M to 5.00 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571)272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jagadishwar R Samala
Examiner
Art Unit 1618

VICKIE KIM
PRIMARY EXAMINER

sjr